UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,506	10/02/2003	Richard J. Melker	UF-378C1	1941

23557 7590 06/08/2005

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER	
DIRAMIO, JACQUELINE A	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,506	MELKER ET AL.	
	Examiner	Art Unit	
	Jacqueline DiRamio	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/11/2005*. 5/27/04, 8/9/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

186

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 - 11, drawn to a method for detecting a target analyte/biomarker, classified in class 435, subclass 4 for example.

II. Claims 12 - 24, drawn to a system useful in the detection of at least one target/analyte, classified in class 702, subclass 19 or 22 for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed in Group II can be used in another materially different process, such as a means for screening potential drug compounds by their binding abilities.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

During a telephone conversation with Margaret Efron on May 11, 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1 - 11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12 – 24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 – 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nanostructure-based assembly with a surrogate marker and means for detecting target analyte/biomarker attached to its surface, does not reasonably provide enablement for a hollow nanotube's release of an entrapped surrogate marker by the uncapping of the nanotube's end-cap through an interaction

between the means for detecting target analyte/biomarker attached to the end-cap and the target analyte/biomarker. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 2 recites the preferred embodiment disclosed in the specifications requiring a hollow nanotube with a surrogate marker within the interior, a closed end, and an end-cap that can be displaced through an interaction between the means for detecting the target analyte/biomarker and the target analyte/biomarker. This displacement of the end-cap is required for the surrogate marker to be released and the detection to occur, but the specification fails to teach one of ordinary skill in the art how to accomplish this displacement. The specifications outline several examples on how to construct a nanotube (p16, 17, 19, and 20) and the ability to attach a suitable end-cap by linkage through various binding, particularly disulfide bonds (p17). The specification further outlines how to "functionalize" the end-caps by attaching the means for detecting target analyte/biomarker, preferably an aptamer, through copolymerization (p24) and methods for loading the surrogate marker into the hollow void of the nanotube (p22). However, Applicant has provided little or no guidance on how the end-cap is removed from the nanotube to release the surrogate marker. Claim 2 broadly recites that the end-cap is displaced when the means for detecting target analyte/biomarker is in the presence of the target analyte/biomarker. On p15 of the specifications, a brief mention is made to a reference for an energy-bearing biomolecular motor, such as an actin-based motor that may be required for the uncapping mechanism. After reviewing the

Dickinson et al. reference, there was no link between the clamped-filament and a nanostructure-based assembly and therefore, it was unclear how this motor could be adapted for use in the nanotube assembly and its end-cap removal. Applicant failed to provide any further references for uncapping mechanisms of the end-cap and no working examples were provided in the specifications to teach the uncapping mechanism.

Therefore, the lack of specific teachings in the specifications as to uncapping the end-cap for the release and subsequent detection of the surrogate marker and the breath of claim 2 for the interaction between the means for detecting target analyte/biomarker and the target analyte/biomarker, which causes the un-capping of the end-cap does not enable one skilled in the art to make and use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: the release of a surrogate marker, which is needed for detection by the sensor technology. The rejection of this claim causes its dependent claims, claims 2 and 5-11, to also be rejected.

Claims 1 – 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as vague and indefinite for the recitation of "sensor technology" because there is a broad range of sensors that could be applicable for this use and it is unclear what sensor technology the applicant is claiming.

Claim 2 is rejected as vague and indefinite for the recitation of "wherein a means for detecting the target analyte/biomarker is in the presence of the target analyte/biomarker, the end-cap is displaced" because it is unclear how "the end-cap is displaced" and if some type of interaction, such as binding, occurs between the "means for detecting the target analyte/biomarker" and the "target analyte/biomarker" to cause this displacement.

Claim 10, "the surrogate marker" lacks antecedent basis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 8 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Fu (US 6,598,459).

Fu anticipates the instant claims by teaching a method for detection of odorant molecules, biological agents or any other chemical or biological species (target analyte/biomarker) in a surrounding fluid. The method utilizes an apparatus comprising a resonator, such as a surface acoustic wave device (sensor technology) coated with a surface area increasing material such as nanotubes (nanostructure-based assembly), wherein the resonator provides a difference in resonating frequencies when contacted with a fluid containing odorant molecules or biological agents (sample of bodily fluid) (see column 3, lines 28-57 in particular). Fu teaches an indirect method to detect the biological agent, through the use of a reactive substance (means for detecting the target analyte/biomarker), such as a protein, reacts with the biological agent resulting in the generation of odorant molecules (surrogate marker) that can then be detected by the invention (see column 3, lines 47-52 in particular). The sensor element in the form of a surface acoustic wave device comprises an oscillator (oscillator circuit), which changes in resonant frequency through interaction with different odorant molecules (surrogate markers). This change in frequency of the oscillator is outputted to a measurement device or frequency shift detector (frequency counter), which is coupled with an intelligent signal processor or artificial neural network (processor) that performs pattern recognition to detect, recognize and identify the odor molecules (surrogate markers) (see column 6, lines 48-65 and column 7, lines 5-63 in particular). Fu teaches the use of the system for detection of all chemical and biological species, but particularly notes

its usefulness for detecting land mines, non-nitrated explosives and explosive liquids (see column 3, lines 11-13 in particular), which are encompassed in the list of Applicant's claim 5. Fu's teaching also allows for the nanotubes (nanoparticle) to be coated with a polymer or equivalent material (means for detecting the target analyte/biomarker) that reacts with the odorant molecules (surrogate markers) or biological agents (target analyte/biomarker), depending if the detection method is direct or indirect, as described above (see column 3, lines 44-52 in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fu (US 6,598,459) in view of Lewis et al. (US 5,571,401).

The Fu reference has been discussed in the 102 rejection above and fails to teach a method comprising combining the nanotubes with a sensor having an array of polymers capable of detecting the presence of a surrogate marker.

Lewis et al. teaches a method for detecting an analyte through a chemiresistor, which comprises sensor arrays coupled to different chemically sensitive resistors fabricated of polymer materials (see column 2, lines 27-39 and column 3, lines 40-56 in particular). The analytes are detected by measuring the change in resistance across the resistors through the use of a measuring device connected to a computer with a data structure of sensor array response profiles and a comparison algorithm. Unknown analytes can therefore be characterized and identified using these response pattern comparison and recognition algorithms (see column 7, lines 45-53 in particular). The sensors taught by Lewis et al. can analyze a wide variety of analytes and fluids by yielding a rapid, low power, dc electrical signal (see column 1, lines 49-57 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the method of Fu comprising a sensor with nanotubes and the sensor technology taught by Lewis et al., because Lewis et al. teach the benefit of using their sensor to detect analytes because of its ability to analyze a wide variety of analytes and fluids by yielding a rapid, low power, dc electrical signal.

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fu (US 6,598,459) in view of Lewis et al. (US 6,467,333).

The Fu reference teaches that their method's detection of analytes can encompass the detection of all chemical or biological species (see column 4, lines 47-53 in particular), but fails to teach that the target analyte/biomarker is specifically selected from the group listed in Applicant's claim 6 and that the bodily fluid sample is specifically selected from the group listed in Applicant's claim 7.

Lewis et al. teach a method of detecting or diagnosing infections, lung cancer, oral infections, and halitosis using marker gases or compounds found in breath samples. In one embodiment, Lewis et al. use volatile sulfur compounds, such as H_2S, for marker gases to diagnose halitosis. H_2S encompasses one of the recited target analytes/biomarkers of Applicant's claim 6. Lewis et al.'s sensor arrays also allow for the identification of various analytes in numerous biological fluids, including breath, blood, urine, feces, saliva, mucus and spinal fluid, which comprise a majority of the list recited in Applicant's claim 7.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the method of Fu comprising the detection of odorant molecules with the specific compounds and biological fluids taught by Lewis et al., because Lewis et al. teach the benefit of using these marker gases to diagnose a variety of infections and diseases.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fu (US 6,598,459) in view of Massey et al. (US 5,866,434).

Fu fails to teach the binding of the surrogate marker and the means for detecting a target analyte/biomarker to a nanoparticle wherein when the means for detecting the target analyte/biomarker is in the presence of the target analyte/biomarker, the surrogate marker is released for detection.

Massey et al. teach a method for assaying an analyte wherein graphitic nanotubes (nanoparticles) are functionalized by attaching a component (means for detecting target analyte/biomarker), such as a binding partner of the analyte of interest, and a label compound (surrogate marker) capable of being induced to luminesce (see column 13, lines 57-67 in particular). To perform an assay, a sample containing the analyte of interest is presented to the functionalized nanotubes wherein the analyte will cleave the component and label compound from the nanotube, causing the label compound to luminesce and be measured through electrochemiluminescence for presence of the analyte (see column 14, lines 20-36 in particular). Massey et al. teach the benefit of using graphitic nanotubes because of their high surface area for immobilization of assay performance substances (see column 6, lines 24-33 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the method of Fu comprising the detection of odorant molecules with the method of functionalizing the nanotubes (nanoparticles) for

subsequent release and detection of a label compound as taught by Massey et al. because Massey et al. teach the benefit using graphitic nanotubes because of their high surface area for immobilization of assay performance substances

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacqueline DiRamio whose telephone number is 571-272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jackie DiRamio
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

05/27/05